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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| EXAMINER | |
|---|---|
| ROOKE, AGNES BEATA | |

| ART UNIT | PAPER NUMBER |
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| 1656 | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/670,563 | KUMPE ET AL. | |
| | Examiner | Art Unit | |
| | AGNES B. ROOKE | 1656 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *14 July 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-13 and 15-24* is/are pending in the application.

4a) Of the above claim(s) *1-9, 16-18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10-13, 15, 19-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

**DETAILED ACTION**

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 07/14/2008 has been entered.

The amendments to the claims have been acknowledged.

***Claim Disposition***

Claims 1-13, 15-24 are pending. Claim 14 is cancelled. Claims 1-9 and 16-18 are withdrawn. Claims 10-13, 15, and 19-24 are examined.

***Objection to Claims***

Claim 13 is objected to because the concentration in line 4 of claim 13 should be expressed in "g/l." Thus, proper correction is required.

***Rejection Maintained***
***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 10-13, 15, and 19-24 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject

matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In *In re Wands*, 8 USPQ2d 1400 (Fed. Cir., 1988) eight factors should be addressed in determining enablement.

1.) The nature of the invention: The claimed invention is drawn to a method for producing a concentrate of factor VIII:C containing vWF comprising fractional precipitation using an alkali metal salt and an amino acid glycine, for example, wherein the concentrate has high molecular weight multimers of vWF and the ratio of ristocetin cofactor to vWF is greater than 1.

2.) The breadth of the claims: the claims are broad because they refer to a process for producing a concentrate of factor VIII:C-containing von Willebrand factor (vWF/FVIII:C) wherein the concentrate has a ratio of vWF:RcoF to vWFAg of greater than 1.

3.) The predictability or unpredictability of the art: / 7.) The state of the prior art: The prior art, Heimburger et al., Factor VIII Concentrate, Highly-Purified and Heated in Solution, Drug Res. 31(I), Nr. 4 (1981) (See original German article and the English translation of the article as attached to this office action), teaches a method that is the same as the instant method wherein a solution is fractionally precipitated using sodium chloride and glycine. See page 3, and Table 1, on page 7, of the English translation. Table 2, of the English translation depicts composition of the factor VIII concentrates and comparison to a commercial product, where the ratio of ristocetin to vWF is less

than 1. See calculation where values were used from Table 2, page 11 of the English translation: FVIII:RcoF=23.6; FVIIIR:Ag/FVIII:C=3; FVIII:C=25; thus FVIIIR:Ag=75 thus FVIII:RcoF/FVIII R:Ag=23.6/75=0.314 thus less than 1.

Therefore, the instant invention is unpredictable because the instant method claimed does not produce a concentrate in which the ratio of ristocetin to vWF is greater than 1 because the prior art reference teaches that the same method steps produce a concentrate in which the ratio is less than 1. Thus, according to the method instantly claimed, it appears that steps to produce a concentrate of ristocetin to vWF greater than 1 are not claimed.

4.) & 5.) The amount of direction or guidance presented:/The presence or absence of working examples: the working examples 1 and 2 and Table 1 on pages 10 and 11, present calculations that a concentrate of ristocetin to vWF is greater than 1.

6.) The quantity of experimentation necessary: there is a large quantity of experimentation necessary to determine whether the method claimed, i.e. a process for producing a concentrate of a vWF/FVIII:C where the concentrate has a ratio of vWF:RcoF to vWF:Ag that is greater than 1, is actually claimed since the prior art by Heimburger et al. clearly teaches the same method that utilizes the same steps where the ratio for the same compositions is less than 1.

8.) Level of skill in the art: the level of skill in this art is high.

In consideration of each of factors 1-8, it is apparent that there is undue experimentation because of variability in prediction of outcome that is not addressed by the present application disclosure, examples, teaching, and guidance presented.

Absent factual data to the contrary, the amount and level of experimentation needed is undue.

Applicants responded that they disagree that the claims are broad when referred to a process for producing a concentrate of factor VIII:C-containing Wilebrand factor (vWF/FVIII:C) wherein the concentrate has a ratio of vWF:RcoF to vWFAg of greater than 1. Further, Applicants state that the Office has failed to consider that the claims are also limited to : (1) alkali metal salts or alkaline earth metal salts; (2) amino acids chosen from glycine, alpha- or beta –alanine, alpha-, beta-, or gamma- aminobutyric acid, lysine, valine, asparagine, and glutamic acid; and concentrates having an increased content of high molecular weight multimers of vWF.

Examiner responds that the enablement requirement is analyzed in view of all of the Wands factors, and not just the factor in regards to the breadth of the claims.

Next, Applicants state that according to the Office, Heimburger establishes the state of the prior art and demonstrates that "the instant invention is unpredictable because the instant method claimed does not produce a concentrate in which the ratio of ristocetin to vWF is greater than 1 because the prior art reference teaches that the same method steps produce a concentrate in which the ratio is less than 1" and that there is a large quantity of experimentation necessary to determine the concentration ratio of vWF:RcoF to vWF:Ag to be greater than 1. Further, Applicants assert that one of the inventive features of the instant invention is the unexpected discovery that the concentration of amino acid used in the fractional precipitation affects whether the

Factor VIII:C- containing von Willebrand factor concentrate exhibits a vWF:RCoF/vWF:Ag ratio that is greater than 1. In addition, Examples 1-4 on pages 9-18 of the specification demonstrates that in all but one case, final concentrations of amino acid in excess of 110 g/l produced vWR:RCoF/VWF:Ag ratios less than 1, whereas ratios greater than 1 were consistently observed when the final concentration of amino acid did not exceed 110 g/l. (See Exhibit A).

Examiner reviewed the specification as originally filed, and nowhere in the specification Applicants claim that the effective amount of any amino acid used in the fractional precipitation is from about 67 to about 110 g/l. The only support in the specification was a teaching that fractional concentration of glycine was from 70 to 160 g/l. (See claim 13 as amended). There is no teaching in the specification that "any amino acid" concentration in the precipitation is from about 67 to about 110 g/l. Therefore, there are no teachings in the specification that would address the effective amount of any amino acid used in the fractional precipitation that has the final concentration of any amino acid in the precipitation from about 67 to about 110 g/l. Further, there is no guidance in the specification to achieve the ratio greater than 1, which is at issue, where the amino acid cannot exceed the final concentration of 110 g/l. Furthermore, claim 13 as amended refers to the concentration of amino acid of about 67 to about 110 g/l and Heimburger uses a glycine concentration that is greater than 110 g/l. Thus, "about 110 g/l" would include numerical values that are greater than 110 g/l and thus being in the range taught by Heimburger.

Additionally, Applicants state that since the claims are currently amended, the examiner's argument stating that "since the steps are the same, the results must inherently be the same" is no longer applicable.

Examiner states that Heimburger and the instant invention teach the same process for producing a concentrate that utilizes the exactly same steps, thus the end product should be identical.

*In re Sussman*, 141 F. 2d 267, 60 U.S.P.Q. 538 (CCPA 1944), provides "that since the steps are the same, the results must inherently be the same unless they are due to conditions not recited in the claims." In the instant case, the claims are drawn to an invention employing the **same process steps** but the product(s) is(are) **alleged to be different**.

Analogously, Heimburger teaches a process of producing concentrate of a factor VIII:C-containing von Willebrand factor (vWF/FVIII:C) when a liquid having factor VIII:C (FVIII:C) and von Willebrand factor (vWF) is fractionally precipitated using at least one of an alkali metal salt and an amino acid glycine. Further, the dissolved precipitate is incubated for 10 hrs at 60°C. See Heimburger on page 6 of the translation.

Identically, in the instant invention, the concentrate of the invention is preferably obtained by fractional precipitation using glycine and an alkali metal salt such as sodium chloride. See example 1 on page 9. Thus, the steps in achieving the concentrate are the same, thus the ratios should be the same. In addition, Heimburger teaches concentration of glycine of greater than 110 g/l and the instant invention claims amino acid concentration of about 110 g/l, thus the numerical values in the same range. Therefore, according to *In re Sussman*, since the steps are the same, the results must inherently be the same unless they are due to conditions not recited in the claims. In the instant case, the claims are drawn to an invention employing the same process steps

but the products, i.e. ratios, are allegedly to be different. Thus, Applicants are required to recite the missing steps to form the alleged different ratios in view of the above-cited decision.

***New Matter Rejection***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 13 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants amended the claim to state that "the effective amount of the amino acid used in the fractional precipitation is such that the final concentration of amino acid in the precipitation is from about 67 to about 110 and the effective amount of the alkali or the alkaline earth metal salt used in the fractional precipitation is such that the final concentration of alkali metal or alkaline earth metal salt in the precipitation is from 100 to 160 g/l." However, this new amendment constitutes a new matter because the specification does not provide information in regards to any amino acids having concentration from about 67 to about 110 g/l, but only has information in regards to glycine that can have such concentration. Further, specification does not teach that any alkali metal or alkaline earth metal salt has concentration of 100 to 160 g/l, but only has

information in regards to NaCl that can have such concentration. Therefore, the new amendment introduces a new matter because there is no support in the specification to address all amino acids and all alkaline or alkali metal salts in this invention.

***Conclusion***

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Agnes Rooke whose telephone number is 571-272-2055. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr Bragdon can be reached on 571-273-0931. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197.

AR

/Karen Cochrane Carlson, Ph.D./

Primary Examiner, Art Unit 1656